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BACILLUS PYOCYANEUS SEPTICÆMIA ASSOCIATED WITH BLASTOMYCETIC GROWTH IN PRIMARY WOUND.

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THE rôle played by the bacillus pyocyaneus in the various pathologic conditions in which it is met has been subject to much discussion and debate. Some maintain that it exists merely as a saprophyte; others maintain, and the weight of recently accumulated evidence would seem to support this view, that it must be considered as a definite etiological factor capable of exciting very diverse morbid phenomena.

The bacillus pyocyaneus was discovered by Gessard in 1882. It was isolated from dressings soiled with so-called blue pus. He regarded it purely as a saprophytic organism which in itself was incapable of producing symptoms in man. In 1889, Charrin published his admirable researches. He was able to produce readily and constantly by injecting the bacillus pyocyaneus into rabbits a condition characterized by a fairly constant symptom complex. Albuminuria, a low grade of fever, diarrhœa, loss of weight, and a spastic paralysis of the hind quarters formed the essential symptom train of Charrin's

"maladie pyocyanique." Autopsy examination showed vasomotor disturbances in the various mucous membranes as well as viscera.

In 1891, Schaefer published in Berlin the results of his experimentation with the bacillus pyocyaneus injected in the dog. His results were quite similar to those published two years before by Charrin.

About this time, Cadeac, working independently of the two observers previously mentioned, published a report of a case of general pyocyaneus infection in a dog. In his case, the point of entrance of the bacillus could not be determined. The animal had died with symptoms of paralysis, diarrhœa, low grade of fever, and profound cachexia. The bacillus pyocyaneus was found in the blood, lungs, spleen, and intestinal tract, post-mortem.

Although the pathogenesis of the bacillus pyocyaneus in lower animals was no longer in doubt, its ability to excite definite morbid phenomena in man was still a matter of dispute.

To Gruber belongs the credit of having first proven conclusively the ability of the bacillus pyocyaneus to produce definite lesions in man. He isolated the organism from a case of middle-ear disease, and reported his findings with such thoroughness as to remove all doubt as to the pathogenesis of this organism towards the human species. Martha about this time also reported two cases of purulent otitis media from which pure cultures of this bacillus were obtained. It has since been found in many parts of the body. The bacillus pyocyaneus is a pyogenic organism. Its most conspicuous rôle is the production of blue pus. However, like the other pyogenic organisms, it can develop in different parts of the body and produce very diverse symptoms.

Its presence in suppurating wounds is not so common as is ordinarily supposed. Jakowski found it only twice in 200 cases. In 800 autopsies held at Johns Hopkins, the bacillus was found in eleven cases. Lartigau found it three times in 100 autopsies.

It has been found in the sweat, in the saliva and sputum,

in fistulous tracts in both large and small intestines, in tuberculous cavities, in the blood in puerperal fever, in the pus of otitis media, in chronic mastitis, in tonsillitis, in diphtheritic inflammation of the œsophagus, in the saliva in noma, in meningeal exudate, in localized infection of the umbilical cord, in the pericardial exudate during life, in a case of tuberculous pericarditis, in ovarian abscess, in bronchial pneumonia, in ureteritis, in pyelonephritis, in intestinal ulceration, in hepatic abscess, in various skin lesions, principally of the ecthymatous type, in furuncle, in panophthalmitis, in ozæna, in acute angina, in bronchiectasis, in gangrene of the lungs, in ulcerative gastritis, in cholera nostras, in infant diarrhœa, in dysentery, in appendicitis, in pericarditis, in peritonitis, in bursitis, in arthritis, in acute endocarditis, in cystitis, in mastitis, in endocervitis, in orchitis, in gangrene of the nose, and in the stomach.

The studies made by Lartigan on an epidemic of dysentery caused by the bacillus pyocyaneus are of great interest and value.

In addition to the above widely diverse conditions caused by the bacillus pyocyaneus, the organism has been shown to produce general septicæmia. Ehlers early published a report of a case of general infection due to the bacillus pyocyaneus. Cases have since been reported by Oettinger, Jadkewitsch, Neumann, Schaefer, Karlinsky, Ledderhose, Krannhals, Kossel, Calmette, Williams, Lavender, Triboulet, Williams and Cameron, Pes and Gradenigo, Le Noir, Kruse and Pasquile, Lartigau, Perkins, and Barker. The authors' case hereinafter described was one of general pyocyaneus infection.

A large number of the cases reported occurred in young children and were characterized by fever varying in degree, profound intoxication, some diarrhœa, and varying nervous phenomena. Most of the cases exhibited small petechial eruptions, from which in a number of the cases the bacillus was isolated during life. In several of the cases, notably Le Noir's and Jadkewitsch's, the bacillus was isolated from the urine during life. However, in the majority of cases, the diagnosis

was made post-mortem. Jadkewitsch's case was particularly interesting. It had many features in common with the authors' case.

JADKEWITSCH'S CASE.—When the case first came under observation, a chronic eczema was noted on both legs. It was very painful, the patient seeking treatment for the relief of this pain. He had had this eczema for ten years. At times it had given him but little trouble, but he had had severe ulcerations in an eczematous patch on his lower right limb several times. At the time the patient presented himself he had but recently recovered from a severe ulceration of his right leg of nearly three months' duration. This ulceration differed from that in previous attacks he had suffered in that the pus was blue, staining the dressing deeply in a very short time. From the report of the case it was evidently a case of typical blue suppuration. The pus gradually disappeared under local treatment, and when first seen by Jadkewitsch was entirely gone, the patient presenting himself for treatment of the chronic painful eczema and for a nervous condition. He had developed paresis with anæsthesia of the whole right arm. This disappeared in seven weeks under appropriate electrical treatment. One month later blue suppuration again appeared, lasting three weeks. It was accompanied by great weakness and emaciation, dyspnœa, a slightly subnormal temperature, and a very rapid pulse ranging from 130 to 145. This lasted for four months, when recovery took place.

Nearly two years later blue suppuration again appeared in the leg. It persisted for four months, with slight intermissions lasting from two to four days. This attack was characterized by diarrhœa, slight elevation in temperature, never exceeding 38.1° C; pulse-rate from 120 to 135, profound prostration, paresis of both legs, and localized disturbance of sensibility. The lips and tongue were anæsthetic. The bacillus pyocyaneus was isolated from the urine by Jadkewitsch. No statement is made in his report whether the organism was recovered from the blood. The patient recovered from this attack, and no subsequent report has been made of the case.

AUTHORS' CASE.—Patient, Miss B., aged seventeen years, American, admitted to hospital December 13, 1903.

Family History.—Father, mother, four brothers, and one sister are living. There is no history of tuberculosis, syphilis, or nervous disease in the family. Patient herself has had the usual diseases of childhood. When nine years old she had measles, with abscess formation in the right ear. She has also had whooping-cough; has had two attacks of pneumonia,—one in the spring of 1902, lasting four weeks, the other in the spring of 1903, when the patient was in bed six weeks; has had slight rheumatism since she was six years old, the attacks usually following exposure, and characterized by sharp pains in the lower limbs and joints.

The patient, a school-girl, has led the usual life of a pupil in a country school. Her habits have been good, and, excepting the diseases of childhood previously mentioned, has, prior to the present illness, been in good health.

On November 18, 1901, in a runaway accident, she was thrown upon a hard macadamized road. She fell on her left side and lay unconscious for fifteen minutes. Upon regaining consciousness she complained of a sharp stinging pain in her left arm, but motion in the arm and fingers, although painful, was possible. Her fingers were numb. She walked to her home, a distance of half a mile. The accident happened on the 18th of the month, but a physician was not summoned until the 21st. At that time her left arm was swollen from fingers to shoulder. There was no discolorization. Movement at the shoulder-joint was normal and painless, but there was great pain when active or passive motion was attempted in the elbow-joint. Muscular power in the hand was decreased. The attending physician applied pressure bandages, but the swelling did not subside. The patient remained in this condition until April, 1903, when she sought treatment elsewhere. The arm was no longer painful, but there was no sensation in the fingers. The arm was now blistered on its outer posterior surface, in all covering an area about two and one-half inches wide by four inches long. No improvement resulted, and soon she became, as the rather unsatisfactory history has it, "completely paralyzed on the left side." She could not move her left arm or leg and had difficulty in swallowing.

She was then taken to Chicago, and was presented in the dispensary clinic of Northwestern University Medical College by Dr. D'Orsey Hecht. After careful examination, the diagnosis of "traumatic hysteria" was returned. She steadily improved under treatment, but returned home in three weeks. On June 19 an operation was performed by her local physician "to relieve pressure on the musculospiral nerve." An incision two inches long was made. The wound healed perfectly. Symptomatically, the operation was not a success, and she was therefore reoperated on July 28.

She soon regained sensation in her hand. The wound healed slowly, and at the end of the fourth week, excepting an area about the size of the end of the little finger, was covered with epithelium. The arm was entirely free from pain and there was no swelling. The wound was dressed with a 10 per cent. iodo-

form gauze dressing. At the end of the fifth week after operation, three small blisters, each about the size of a millet-seed, developed in the small area of granulating tissue still uncovered with epithelium. These rapidly increased in size, and in twenty-four hours became confluent, covering the entire granulating area. In a few hours, the one large blister broke, discharging a thin, clear, watery substance. The process was extremely painful and abrupt in onset.

Mode of Onset.—She was seized with a slight rigor accompanied by great pain in the region of the wound. The pain was at first of a boring character. It soon changed to a dull burning, and was so severe that two repeated hypodermatic injections of morphine sulphate, grains one-quarter each, were given. She complained of heat and soreness in the skin surrounding the area visibly involved. There was no itching or cracking of the skin. By the fifth day, a round area a little larger than a twenty-five-cent piece was involved. It was "one big blister," which broke and refilled every four or five hours. The discharge now assumed a grayish tinge. She was at this time in great pain, but not delirious or prostrated.

On the sixteenth day the wound took on a blue tint. In a few hours the entire surface was of light blue color. Blisters no longer formed, but the surface exuded a thin, watery fluid. This was tinged blue, and the dressings when removed were quite deeply stained. The wound was curetted and carbolic acid (5 per cent. solution) applied locally. The dressing was changed once every hour. However, in spite of all treatment, the condition gradually spread, until in seven weeks an area as large as the palm of the hand was involved. At times it was light blue, then darker blue, portions becoming dirty brown. All shades from light blue to the dirty brown could be seen in the wound at once. The discharge remained watery and thin and of blue color.

About two weeks after the appearance of the blue discharge she began to feel "a general uneasiness." She started violently and jumped at the slightest sound. The opening of a door caused her to shake with fear. This was followed by a feeling of dizziness. She had severe headache that lasted for hours, and complained continuously of severe pain in the back of her head. She answered questions intelligently, but was unable to remember. Her face, arm, and leg muscles twitched involuntarily. In all, she was profoundly prostrated.

The wound on the arm resisted all efforts to heal it. It was curetted and strong antiseptics applied, but the blue film would return in a few days, even under frequently changed and strong moist bichloride dressings. The X-ray was used for two weeks, a low vacuum-tube being applied four inches from the wound every other day for ten minutes. The wound was canterized with the Paquelin cautery, the diseased tissue burned out; the cauterization being carried well beyond the seeming margin of the ulcer and deeply below the base. However, nothing had been of marked benefit, the process being entirely unaffected by the X-ray treatment, and recurring quite promptly after the canterization. The wound was again curetted and pure carbolic acid applied, this also without benefit, the condition returning inside of a week as seriously as ever. The pain in the arm was so great that morphine was given frequently. The chronicity of the condition was distressing to the patient and her family, largely because of the extreme and steady pain, and it was for the relief of this that she determined to have the arm amputated, coming to the hospital for this purpose.

Status at the time case first came under the writers' observation. Patient very weak; unable to walk without being supported. Mother stated her normal weight to be 135 pounds. She then weighed ninety-two pounds. She walked with an unsteady, reeling gait, but stated that she was not dizzy. She tired on the least exertion. She had no cough. Her appetite was fitful; at times she desired food, but eating generally nauseated, and frequently caused vomiting. She had been markedly constipated, sometimes having had only one scanty bowel movement a week.

Urination had been difficult at times, and some time previously she had been catheterized for a whole week. Urination was never painful; she was simply physically unable to evacuate the bladder.

Menstrual History.—Began at fifteenth year, normal in every way until November 3, 1903, when menses ceased. This phenomenon has not appeared since.

Body in General.—Slender frame, height five feet one inch, symmetrical, no anomalies of development, musculature good but flabby, panniculus adiposus poor, large and heavy bones.

General State.—Markedly depressed; she answered questions in a disconnected manner, and was not interested in her surroundings. She seemed almost in stupor, it being difficult

to arouse her. Occasionally she uttered a low moan. She had not been delirious. She lay in the same position for half an hour at a time, not attempting to arrange herself comfortably, even though the position assumed be an uncomfortable one. She had slept but little for several weeks, the extreme pain in the arm and head making it impossible. She complained of a dull ache in the back of her head. Temperature and respiration normal; pulse, 101.

Skin.—On the face, body, and lower limbs clear and of good color, but cold and moist. There were no scars or eruptions. Skin of left arm on its entire outer surface was bronzed, due to the use of the X-rays in treating the local ulcer. On the outer anterior surface of the left arm, occupying an area about the size and shape of the palm of the hand, was a large ulcer, its margins sharply defined and indurated, and the whole slightly elevated. The base of the ulcer was blue, the shade of blue varying in different parts of the ulcer; in some portions being light sky-blue, in others darker blue, while some areas were brown. The light blue areas were bathed with a thin watery fluid which stained the dressing blue. The fresh stains of the dressing were of a light shade of blue, but after half an hour's exposure to air the color changed to a darker blue (about the shade of Loeffler's methylene-blue solution). The brown areas were dried, hard, and firm. There was little or no exudation from these areas. They consisted of thin, very adherent crusts, the surface bleeding quite freely if irritated.

Scrapings were made from the surface of the wound and stained in Loeffler's methylene blue. The following rough findings were made at this preliminary examination:

Light Blue Areas.—An exudation from one to three millimetres thick extended over these areas.

The exudation was moist, and was readily removed with the platinum loop, causing no bleeding.

In consistence it resembled the scraping obtained from a caseated bronchial gland.

Dilution drops were made and cover-glass smears were stained with Loeffler's methylene blue. They took the stain readily. In these, upon examination, were found a large number of blastomycetes. They consisted of a central cell-body about the size of a red blood-cell surrounded by a capsule of equal thick-

ness. The capsule did not take the stain readily, but in a number of cases the outside rim of the capsule stained faintly. There were a few small bacilli in these sections and masses of detritus taking a heavy deep blue stain.

Brown Areas.—In the brown areas, scrapings were obtained with difficulty. The exudate was hard and dry and very adherent, so much so that when a portion was broken off for examination the denuded area bled freely. Examination of the scrapings of this area showed a few blastomycetes, all of them in a budding state. No bacteria were seen.

The wound was extremely painful, and the small amount of manipulation necessary in obtaining the scrapings caused great discomfort. Examination of the lungs, heart, and abdomen was practically negative. The spleen could easily be palpated. It was markedly increased in size, extending a full inch below the ribs with the patient in the reclining position. No enlarged lymphatic glands could be felt, but tenderness was present in the pit of the left axilla. There was neither redness nor œdema in this axilla.

The patient was placed under close observation and vigorous saline catharsis begun. Moist dressings of bichloride of mercury, 1–5000, were applied, the dressings being changed every half-hour day and night. There was no increase in temperature, although the pulse-rate was high.

The local condition on the arm did not improve. On December 15, under a general anæsthetic, the blue slough was removed, great care being taken not to button-hole the surface taken off or infect the fresh tissue with the area being removed. A fresh, clean surface was thus obtained. Moist bichloride-of-mercury dressings, 1–2000, were applied, and the dressing changed once an hour. The patient's mental condition improved at once. She became more cheerful; she no longer experienced the violent pains in her arm and head, answering questions readily. The wound on the arm was soon covered with healthy granulations. The base of the wound was largely composed of tissue of the cut arm muscles. These muscles could be seen occasionally to jerk and twitch. This was not painful.

On January 4 the patient sat up. She had been free from pain in the arm since the operation, made three weeks previously, and the granulating area on the arm was free from blue pus. The

wound was covered with an ordinary dry dressing and bandage. She attired herself in the dress which she had worn when she entered the hospital, and in a very few hours was seized with a violent chill. The abruptness of the onset was marked. A distinct chill lasting for about half an hour was followed by profuse sweating. Her arm at once became very painful. The bichloride dressings had been continued without interruption from the time of operation. Examination at this time was negative. Three hours later the arm was re-examined, and three small blue spots the size of pin-heads were seen. These were in the centre of the granulating area, and none were nearer than half an inch to the margin of the wound. These areas were carefully cut out and the spots cauterized with pure carbolic acid. However, the girl became more and more depressed.

Bichloride-of-mercury dressings, 1–3000, were now applied and changed every twenty minutes. The process spread rapidly in spite of this, and in ten hours the entire area of granulation was covered with a light blue membranous exudate, staining the dressings bright blue a few minutes after they were applied. The patient refused food, complaining continuously of the pain. The temperature remained normal or slightly subnormal. The pulse was rapid, ranging from 90 to 120, and of a light thready character. Stupor was very pronounced, at times it being almost impossible to arouse her. She did not become emaciated.

Cultures were made from the surface wound, January 7. The plates were developed at ordinary room temperature, which was hardly more than 65° F. The growth on the plates was slow.

1. On the third day, small grayish pin-point colonies appeared. Under low magnification these colonies were seen to be roundish in shape, with faintly defined borders. In the centre was a dark mass. The periphery shaded off into the medium, the whole being granular. There was no liquefaction. Agar-agar, glycerin-agar, and gelatin cultures were made. When the cultures and plates were taken into a warm room, the growth was very rapid. In twenty-four hours the colonies attained a diameter of from one-quarter to three-quarters of an inch, and liquefaction progressed rapidly, the centre becoming liquefied first.

2. On the eighth day, colonies of another variety appeared. They were round, elevated, and about half the size of a small millet-seed. They did not liquefy. Stab gelatin cultures and agar-agar and glycerin-agar cultures were made.

Cultures.—Colony 1. The growth from colony 1 proved to be that of the bacillus pyocyaneus. The growth was characteristic, liquefying gelatin rapidly and developing in funnel form. Green coloring matter (pyocyanine), soluble in chloroform, developed after the fourth day. After seventeen days all the gelatin was liquefied, and the culture was simply a mass of light greenish-colored fluid. This gradually darkened and became brown. On agar-agar and glycerin-agar a gray surface growth developed along the line of scrapings with the platinum loop. The growth was distinctly grayish and remained of this tint. At the eighth day the medium began to be tinted a faint green. The coloring extended far out into the medium from the surface of the growth. After two weeks, the entire mass of the medium was tinted a bright green. The growth, however, remained grayish.

Morphology.—With hanging drop and oil immersion the organism could be seen to be rapidly motile. It stained with ordinary aniline dyes and was a short bacillus with rounded ends.

Colony 2. The organism grew slowly in gelatin, no colonies appearing until the ninth day. The growth was along the entire line of the stab puncture and was greatest at the surface. It tended to spread over the surface of the gelatin. There was no liquefaction.

Cultural Characteristics.—Stab cultures in gelatin developed a growth along the entire line of puncture at ordinary room temperature. There were no gas bubbles, nor did liquefaction occur at any time. The organism developed slowly. Involution forms appeared. On the sixth day after the first appearance of the growth, two series of transplantations were started, one in which a new culture was made every four days and one in which a new culture was made every three days. The growth transplanted every four days lasted twelve generations, when it ceased to develop. The growth transplanted every three days lasted nineteen generations, when it ceased to develop. At the third generation in each series, the individual cell lost its capsule and became irregular in shape, varying from a round body, about half the size of a red blood-cell taking a deep stain, to an irregular oval body, the long diameter of which was about the size of a white blood-cell. The cells grew smaller and smaller, and in the ninth generation looked like a zooglia mass of irregularly shaped cocci, taking, however, a deep nuclear stain. Individual cells,

when seen separate and apart from a mass collection, did not show a capsule. On agar-agar (neutral reaction) and agar-agar litmus (alkaline) no growth developed. On glycerin-agar growth developed on the twelfth day and died out in three generations.

An attempt was made to grow the organism on wort gelatin; the results, however, being less encouraging than with plain nutrient gelatin, the organism dying in the fourth generation. The organism apparently developed as readily under practically anaërobic as aërobic conditions. A tube of gelatin was taken and inoculated as in an ordinary stab culture, and the contents of another tube of gelatin melted at a low temperature and poured in over the surface of the tube previously inoculated. A growth appeared in the deep portion one and one-half inches from the surface of the gelatin in nine days.

Morphology.—The organism stained readily with the ordinary aniline dyes, and was found to be about the size and shape of a red blood-cell, taking a very deep stain. Each cell was surrounded by a capsule of about the same thickness as the deeply stained portion of the cell. The capsule did not take the stain except at its outer margin, which stained faintly. The capsule was best demonstrated by the following technique:

1. Specimen stained in carbol fuchsin for five minutes, raising the stain to the boiling-point.

2. Washed thoroughly in water.

3. Decolorized for two minutes in one-half per cent. solution of hydrochloric acid in 80 per cent. alcohol.

By this technique the cell-body was stained deep red, but not so deeply as to mask the cell structure. Care was taken, however, in decolorizing not to completely remove the stain from the cell. By carefully decolorizing, the cell-body was seen to be highly granular with light unstained areas. No reticulum could be made out. The capsule stained a delicate pink, the outer margin of the capsule taking a distinctly darker tint. The stain was not permanent, the pink in the capsule disappearing in a few weeks. However, the rim of the capsule and the deep staining cell-body remain stained after two months.

The ordinary budding forms of blastomycetes were found after the third day in the culture.

On January 10, petri-dish plates were made from the blood.

Technique.—A. The ball of the thumb of the right hand (the ulcer was on the left arm) was carefully scrubbed with green soap and a stiff brush for fifteen minutes.

B. Washed with sterile water for ten minutes.

C. Washed in 95 per cent. grain alcohol for ten minutes.

D. Soaked in solution of bichloride of mercury, 1–1000, for ten minutes.

E. Washed in normal salt for fifteen minutes.

F. Washed in sterile water for fifteen minutes.

Surface of the thumb was scraped carefully with platinum loop and four petri-dish control plates were made. The thumb was then lanced and a free hæmorrhage obtained. The first few drops were removed with filter paper previously sterilized. Five petri-dish preparations were then made as follows:

Plate 1. Five drops of blood in a tube of three inches of gelatin.

Plate 2. Seven drops of blood in a tube of gelatin three inches deep.

Plate 3. Nine drops of blood in a tube of gelatin three inches deep.

Plate 4. Eleven drops of blood in a tube of gelatin three inches deep.

Plate 5. Twelve drops of blood in a tube of gelatin three inches deep.

Findings.—No growth of any kind developed on the plates made from the skin. Plates 2, 4, and 5 developed colonies which were alike in all cases. They were small and round,—grayish in color,—and grew rapidly at ordinary room temperature. After thirty-six hours they began to liquefy at the edge, and in four days the medium immediately around each colony was tinted a light bright green. Cultures were made from the colonies. They grew quite readily on agar-agar, glycerin-agar, and nutrient gelatin.

Growth in Gelatin.—This growth was rapid in its development, growing in the characteristic funnel fashion. Liquefaction began on the third day. On the fourth day a green tinge could be observed spreading out into the medium from the growth. In a week, the entire mass of unliquefied gelatin was tinged a bright green. Soon the entire mass of gelatin was liquefied and the entire liquid mass was green, but gradually grew darker and

darker, finally becoming brown in color. Before the mass became entirely liquefied, the green color was confined to the unliquefied medium, the flocculent growth being grayish and absolutely devoid of green.

On glycerin-agar and agar-agar the growth developed rapidly along the line of smear. In seven days the medium immediately beneath the growth was tinted green, the green spreading into the medium with great rapidity. In a week the entire medium was tinted green, but the growth was grayish, and remained so throughout, never acquiring the green tint so plainly seen in the medium. The organism was developed at ordinary room temperature.*

Morphology.—The organism proved to be a small bacillus with rounded ends about two and one-half to three times as long as wide.

Hanging-drop preparations showed a motile organism. Motion was lost after two days' growth in gelatin. Staining for spores gave a negative result. The organism, from its cultural and morphological characteristics, was identified as the bacillus pyocyaneus. Cultures were made following the technique de-

* We are aware that the technique used above is not the most approved one for making a bacteriological examination of the blood. We did not have on hand at that time the large quantity of bouillon necessary, so we did not draw off blood in a syringe and inoculate a large quantity of bouillon with a small quantity of blood, as is the usual method. However, the usual method, it seems to us, is preferable to the method used, only in that it is more liable to yield positive findings. By the use of the large quantity of gelatin, we in a way diluted the blood, and thus reduced to a certain extent the possible bactericidal action of the blood, which after all is one of the chief virtues of the methods in which large quantities of bouillon are used. Positive findings are of value, no matter what the technique, providing, of course, they are not subject to objection on the ground of inaccuracy. Great care was taken in every step in preparing the thumb to remove the possibility of contamination with organisms upon the skin, and we feel that the thumb was as aseptic as it is possible to render the living tissue. The non-development of the five control cultures made from the skin at the point of withdrawal adding evidence to our belief that there were no germs on the skin. The bichloride was mechanically, instead of chemically, removed by the normal salt and water, much time being taken and a large volume of fluid being used, so that we feel that the failure to obtain any growth from the skin scraping was not due, as is often the case, to a small amount of the bichloride being carried into the medium.

scribed above on January 14, 17, 20, 24, and 26. The drops were taken from different portions of the body each time and control cultures made in every case. In every instance the control culture failed to develop. On the 14th, 17th, and 20th, a pure culture of the bacillus pyocyaneus was obtained, but on the 24th and 26th we were unable to grow cultures. On the 26th only one petri-dish showed any development, it being the one in which there were twelve drops of blood, only one colony developing. In the preparation taken on the 24th and 26th there were no developments.

Urine Examination.—The urine was examined frequently, the following being a report of the first examination made.

Reaction, acid.

Specific gravity, 1027.

A. Soluble constituents.

1. Albumen test.
   a. Nitric acid and heat, positive.
   b. Acetic acid and ferrocyanide, positive.
2. Sugar.
   a. Fehling's and Boettgar's tests, both negative.
3. Bile.
   a. Iodine and Jolles' tests, both negative.
4. Diazo reaction, absent.
5. Acetone, absent.
6. Urea, quantitative estimation, normal.

B. Sediment, small in amount; composed largely of calcium oxalate crystals.

Examination was made daily. A varying amount of albumen was present; otherwise, the examinations were negative.

Blood Examination.—Marked leucocytosis was present, mostly of the polymorphonuclear variety. A few eosinophiles were seen. There was poikilocytosis.

These findings were of unusual interest in view of the symptom complex observed. The patient was evidently suffering from an acute intoxication of severe grade. She had no elevation of temperature; in fact, her temperature may be said to have been uniformly subnormal. Her respiration had been high, varying from 25 to 35, and her pulse small and running between 90 and 130. The most marked symptom was the marked degree of mental hebetude. There had been profound stupor for many weeks, at times approaching coma. Although the element of

hysteria was to some degree in evidence in the patient, it could hardly account for the profound depression and lack of ordinary intelligence. She was not marasmic. Removal of the only discoverable inflammatory focus, the ulcer on the arm, while it gave relief from the pain, did not completely relieve the pronounced symptoms of the toxæmia, the patient being restless and prostrated as before.

Treatment.—It is an interesting fact that the use of serum from immunized animals as a therapeutic measure has been proven to be of value in infections with the bacillus pyocyaneus; in fact, Bouchard prepared and used successfully an antipyocyanic serum four years before Behring gave to the world diphtheritic antitoxin. Bouchard's method of preparing the serum was very simple. A healthy rabbit was selected and inoculated with a sterile beef-tea culture of the bacillus pyocyaneus. This produced a slight reaction. The rabbit was then successively inoculated with increasingly stronger cultures of the living organism in the usual manner until an immunity was produced protecting it against an inoculation which otherwise would have been rapidly fatal to an unimmunized animal. Blood was then withdrawn and the serum secured in the usual manner. This serum was not only protective, but curative. It took about seven months to develop in an animal an immunity yielding a serum of value.

This serum, however, is not an article of commerce, and could not be found on the market, nor could any be obtained from any of the large biological laboratories. The case was therefore treated symptomatically.

A study of the reported cases of local infection by blastomycetes shows that the treatment giving most favorable results consists in the use of large doses of potassium iodide.

The patient was given fifteen drops of potassium iodide well diluted every three hours. Under ether anæsthesia the sloughing mass on the arm was excised. Ichthyol (10 per cent. in glycerin) was applied locally to the wound, the dressing being moistened with fresh solution every hour and changed every four hours. The application was non-irritating and, excepting the offensive odor, was agreeable to the patient.

On the third day after the operation she again complained of pain in the arm. The pain was not so great as it had been, yet was such as to cause fear on the patient's part lest a recurrence develop. Examination revealed nothing; the ichthyol discoloring the surface and masking it. On the sixth day, examination showed the margin of the wound to be hard and indurated. The patient complained continually of pain in the part, and, although examination revealed but little, the surface being masked by the ichthyol, there could be no question but that a recurrence had appeared.

The girl became decidedly more nervous and irritable. She jerked and twitched, and of necessity was watched to prevent her escape from bed. The pain in the arm became so intense that morphine sulphate, grains one-eighth, were given hypodermatically every three hours. This did not suffice to entirely relieve the pain. The pulse was high and rapid, ranging from 94 to 115. Her temperature ranged from 96.7° to 98.2° F. Only once did it reach 99°. Both temperature and pulse were lowest in the morning and reached their greatest height in the afternoon.

On January 20 it was necessary to discontinue the potassium iodide, as it could no longer be retained. An elixir of salicylic acid ten grains to the drachm was substituted, one drachm being given every four hours. This was well borne by the stomach. In three days, tincture of chloride of iron, drops fifteen three times a day, was added. However, the pain in the arm steadily increased, so that in twelve hours seven-eighths of a grain of morphine had been given her without relief from the pain. It was now decided to return to the potassium iodide, and ten drops were given every two hours. In three days the pain left the arm, and, although restless, nervous, and irritable, the girl did not seem to be in pain. The tincture of chloride of iron and the saturated solution of potassium iodide with local application of the 10 per cent. ichthyol were continued until the patient left our observation. The wound in the arm began to heal. When she left the institution, the wound was circular, with a diameter of about one-half inch. The margins were soft and the base on a level with the surrounding skin. She was sent to her local physician, with the recommendation that the treatment (frequently repeated large doses of potassium iodide and tincture of chloride of iron together with a local application of 10 per cent. ichthyol in glycerin) be continued. In a recent letter he states that the

wound is completely covered over with healthy normal epithelium, excepting an area as large as the nail of the little finger. He has reduced the dosage. The patient herself is leading an active out-door life and is apparently well.

While the patient was in the hospital her mother called. She stated that she had been "troubled with boils." Six weeks previously she had noticed a small, hard lump develop on the back of her left hand. It was about the size of a pea when she first noticed it. It gradually grew larger, until it reached the size of a small pigeon egg, when it gradually disappeared. At no time was it painful, nor was the overlying skin reddened or tender. It did not soften and break as she had expected it to do, but remained hard, gradually becoming smaller until it entirely disappeared. She did not open it nor break the skin. A few days after this had entirely disappeared, she noticed on the point of her elbow a hard, round body about the size and shape of a marble with a diameter of about half an inch. She herself states that it felt exactly like the growth which had appeared upon her hand. It was not painful or tender and had been there for some time, she thought, before she discovered it. It increased in size slowly, and on the advice of a friend she opened it with a needle. A thin, grayish, watery substance was discharged. Examination of the discharge showed it to contain blastomycetes in the budding form in great numbers. The budding was very marked; in fact, there were very few cells seen which did not show some budding. Examination of the axilla revealed a large, hard mass about the size of a hen's egg. The patient did not know it was there, as it was not painful and did not cause the slightest inconvenience. She was put upon potassium iodide and sent home.

The discharge in the elbow subsided shortly, but the large mass in the axilla broke, and discharged, according to the patient's statement, nearly two cupfuls of a thin, watery, grayish substance. No examination was made of the substance discharged. The patient has continued the use of potassium iodide, but she still has a discharge in the axilla. The patient stated at the time of examination that her son, a nineteen-year-old boy, had a similar discharge from his hip. A small kernel had developed to the size of a large hen's egg, had broken and discharged a thin, watery content similar to that seen in the mother. It had broken some three months before, but was still discharging. This is of peculiar interest in that we have three cases of blastomycetic

infection in the same family. In the mother and brother there was no apparent involvement of the skin and no pain, although in the sister this was quite marked.

Conclusions.—The interesting features of this case suggest the following conclusions:

First. There existed a general septicæmia caused by the bacillus pyocyaneus. The clinical manifestations were not such as would lead to the complete diagnosis, this resting entirely upon the bacteriological findings. There was every evidence of profound intoxication. It was accompanied by a very high pulse-rate with a temperature usually subnormal. Most of the cases heretofore reported have shown some elevation of temperature, with pulse-rate not so high as in the authors' case.

Second. Probably the most marked feature, and certainly one of diagnostic value, was the marked nervous involvement. It has been demonstrated that pyocyanine injected into guinea-pigs produces marked and violent convulsions. Large doses were fatal, while smaller doses produced an increased nervous irritability. In many respects the case is similar to Jadkewitsch's.

Third. The finding of blastomycetes in the local ulcer at once cleared our diagnosis, and explained the failure of the wound to heal. The combination of the blue pus bacillus infection with the blastomycetic infection was unusual. We have been unable to find any report of another similar instance in literature.

Fourth. We had in this case a clean incised wound healing by first intention. The wound became infected with blastomycetes primarily, with the bacillus pyocyaneus secondarily. Many cases of wound infection have been observed due to the bacillus pyocyaneus; but the ability of blastomycetes to infect clean wounds and produce delay of union, with destruction of tissue, is not generally recognized. While the complication is rare, owing to the limited distribution of pathogenic yeasts, still it should, we feel, be given more consideration than is now accorded it.